

WEST Search History

DATE: Wednesday, February 23, 2005

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
<i>DB=PGPB,USPT; PLUR=YES; OP=OR</i>			
<input type="checkbox"/>	L11	reinl-\$\$.in.	9
<input type="checkbox"/>	L10	l8 not 15	4
<input type="checkbox"/>	L9	l8 not 15L8	8
<input type="checkbox"/>	L8	degenerate same linker same triplet same repeat\$	8
<input type="checkbox"/>	L7	L6 not 11	1
<input type="checkbox"/>	L6	degenerate same linker same (triplet with repeat\$)	5
<input type="checkbox"/>	L5	library same linker same (triplet with repeat\$)	8
<input type="checkbox"/>	L4	linker same (triplet with repeat\$)	20
<input type="checkbox"/>	L3	L2 not 11	4
<input type="checkbox"/>	L2	linker same degenerate same triplet same repeat\$	8
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>			
<input type="checkbox"/>	L1	(linker with library) same degenerate same triplet same repeat\$	5

END OF SEARCH HISTORY

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
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NEWS 3 SEP 01 New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS 4 OCT 28 KOREPAT now available on STN
NEWS 5 NOV 30 PHAR reloaded with additional data
NEWS 6 DEC 01 LISA now available on STN
NEWS 7 DEC 09 12 databases to be removed from STN on December 31, 2004
NEWS 8 DEC 15 MEDLINE update schedule for December 2004
NEWS 9 DEC 17 ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS 10 DEC 17 COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS 11 DEC 17 SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS 12 DEC 17 CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS 13 DEC 17 THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS 14 DEC 30 EPFULL: New patent full text database to be available on STN
NEWS 15 DEC 30 CAPLUS - PATENT COVERAGE EXPANDED
NEWS 16 JAN 03 No connect-hour charges in EPFULL during January and February 2005
NEWS 17 JAN 26 CA/CAPLUS - Expanded patent coverage to include the Russian Agency for Patents and Trademarks (ROSPATENT)
NEWS 18 FEB 10 STN Patent Forums to be held in March 2005
NEWS 19 FEB 16 STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FILE 'HOME' ENTERED AT 19:55:41 ON 23 FEB 2005

=> fil medline biosis caplus embase wpids
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 0.21 | 0.21 |

FILE 'MEDLINE' ENTERED AT 19:55:58 ON 23 FEB 2005

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FILE 'CAPLUS' ENTERED AT 19:55:58 ON 23 FEB 2005
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=> e reinl stephen?/au
E1 2 REINL STEPHEN/AU
E2 14 REINL STEPHEN J/AU
E3 0 --> REINL STEPHEN?/AU
E4 1 REINL STEVE/AU
E5 41 REINL W/AU
E6 4 REINL WALTER/AU
E7 1 REINLAEND W/AU
E8 1 REINLAENDER H/AU
E9 1 REINLAENDER HEINZ/AU
E10 1 REINLAENDER P/AU
E11 2 REINLAENDER WALTER/AU
E12 1 REINLAND T L/AU

=> e1 or e2
L1 16 "REINL STEPHEN"/AU OR "REINL STEPHEN J"/AU

=> l1 and linker
L2 6 L1 AND LINKER

=> dup rem l1
PROCESSING COMPLETED FOR L1
L3 13 DUP REM L1 (3 DUPLICATES REMOVED)

=> l3 and linker
L4 4 L3 AND LINKER

=> t ti 14 1-4

L4 ANSWER 1 OF 4 MEDLINE on STN
TI Individualized human scFv vaccines produced in plants: humoral
anti-idiotype responses in vaccinated mice confirm relevance to the tumor
Ig.

L4 ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI Individualized human scFv vaccines produced in plants for the treatment of

Non-Hodgkin's Lymphoma: Anti-idiotype responses in vaccinated mice confirm relevance to the tumor Ig.

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
TI Self antigen vaccines for treating B cell lymphomas and other cancers

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
TI Oligonucleotides of variable length and sequence for use as **linker** regions for dual-domain or multi-domain molecules

=> d ibib abs l4 1-4

L4 ANSWER 1 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2003464247 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12957399
TITLE: Individualized human scFv vaccines produced in plants:
humoral anti-idiotype responses in vaccinated mice confirm
relevance to the tumor Ig.
AUTHOR: McCormick Alison A; **Reinl Stephen J**; Cameron
Terri I; Vojdani Fakhrieh; Fronefield Michele; Levy Ronald;
Tuse Daniel
CORPORATE SOURCE: Large Scale Biology Corporation, Vacaville, CA 95688, USA..
alison.mccormick@lsbc.com
CONTRACT NUMBER: CA33399 (NCI)
SOURCE: Journal of immunological methods, (2003 Jul) 278 (1-2)
95-104.
Journal code: 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20031008
Last Updated on STN: 20031031
Entered Medline: 20031030

AB We have developed a method for rapidly producing in plants the idiotype regions of the tumor-specific Ig as single-chain Fv (scFv) proteins for use in the treatment of non-Hodgkin's lymphoma. Variable region gene sequences were generated from either a tumor hybridoma or human tumor biopsy cells, and idiotype domains were joined by a novel **linker** and cloned into a modified tobacco mosaic virus (TMV) vector designed to secrete the scFv protein in infected Nicotiana benthamiana plants. Thirty-eight out of 44 human scFv proteins showed Coomassie visible material in crude secretory (interstitial fluid, IF) extracts, 21 of those between 100 and 800 microg/ml. Eight of these proteins were tested for appropriate idiotype responses in vaccinated mice. In all eight cases, anti-idiotype immune responses were induced with minimal cross reactivity to irrelevant Ig or scFv proteins. Four out of four anti-scFv sera were also shown to recognize the Ig on human tumor cells by flow cytometry analysis.

L4 ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:241217 BIOSIS
DOCUMENT NUMBER: PREV200200241217
TITLE: Individualized human scFv vaccines produced in plants for the treatment of Non-Hodgkin's Lymphoma: Anti-idiotype responses in vaccinated mice confirm relevance to the tumor Ig.
AUTHOR(S): McCormick, Alison A. [Reprint author]; **Reinl, Stephen** [Reprint author]; Cameron, Terri [Reprint author]; Levy, Ronald; Tuse, Daniel [Reprint author]

CORPORATE SOURCE: Large Scale Biology, Corp, Vacaville, CA, USA
 SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp.
 466a. print.
 Meeting Info.: 43rd Annual Meeting of the American Society
 of Hematology, Part 1. Orlando, Florida, USA. December
 07-11, 2001. American Society of Hematology.
 CODEN: BLOOAW. ISSN: 0006-4971.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 17 Apr 2002
 Last Updated on STN: 17 Apr 2002

AB The use of idiotype vaccines or the treatment of Non-Hodgkin's Lymphoma (NHL) has proven effective in the clinic, and yet has not reached widespread application due to the difficulty in producing individualized Ig proteins from the patients' B-cell tumors. We have developed a method to rapidly produce the idiotype regions of the tumor-specific Ig as single-chain Fv protein (scFv; McCormick, et al., PNAS 1999 96(2):703-708). cDNA is made from a patient's tumor RNA, and then PCR amplified with nested primer sets to generate the tumor variable region gene sequences. Gene-specific primers and PCR are used to generate an scFv library, which is then cloned directly into a modified TMV (tobacco mosaic virus) vector for expression in plants. By randomizing the **linker** between the variable region gene sequences and screening a small population of **linker** variants in infected plants, patient-specific scFv proteins can be made that retain the tumor Ig idiotype and are optimized for expression, stability and secretion. Of the human scFv proteins tested, greater than 90% showed Coomassie-visible bands in crude plant extracts. For a subset of 8 scFv constructs, scFv protein was purified from plant extracts, and then evaluated for induction of appropriate anti-idiotype responses in vaccinated mice. Sera from all eight human scFv-vaccinated mice contained antibodies that recognized the tumor Ig by Western or ELISA. Additionally, four different anti-human scFv anti-sera were shown to recognize the Ig on autologous human tumor cell by FACS. These data suggest that scFv proteins expressed in plants are folded correctly, without the need for denaturation, and accurately represent the tumor idiotype. This method of individualized vaccine production is rapid, yielding vaccine protein in weeks, and fully scalable, suggesting that idiotype vaccination using scFv proteins instead of whole Ig may be feasible using a TMV-based transient plant expression system. A Phase I clinical trial using scFv protein vaccination for the treatment of NHL is currently in progress.

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2001:693353 CAPLUS
 DOCUMENT NUMBER: 135:271876
 TITLE: Self antigen vaccines for treating B cell lymphomas
 and other cancers
 INVENTOR(S): Reinl, Stephen J.; Turpen, Thomas H.
 PATENT ASSIGNEE(S): Large Scale Biology Corporation, USA; McCormick,
 Alison A.; Tuse, Daniel
 SOURCE: PCT Int. Appl., 89 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2001068682 | A1 | 20010920 | WO 2000-US28362 | 20001013 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU,
 ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 US 2003044417 A1 20030306 US 2000-539382 20000331
 CA 2402086 AA 20010920 CA 2000-2402086 20001013
 EP 1263779 A1 20021211 EP 2000-973516 20001013
 EP 1263779 B1 20041215
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL
 JP 2003527399 T2 20030916 JP 2001-567772 20001013
 AT 284897 E 20050115 AT 2000-973516 20001013
 US 2003035807 A1 20030220 US 2002-67790 20020208
 US 2003039659 A1 20030227 US 2002-67892 20020208
 US 2003044420 A1 20030306 US 2002-67893 20020208
 ZA 2002006798 A 20030826 ZA 2002-6798 20020826
 PRIORITY APPLN. INFO.: US 1999-155979P P 19990924
 US 2000-522900 A 20000310
 WO 2000-US28362 W 20001013

AB A polypeptide self-antigen useful in a tumor-specific vaccine mimics one or more epitopes of an antigen uniquely expressed by cells of the tumor. The polypeptide is preferably produced in a plant that has been transformed or transfected with nucleic acid encoding the polypeptide and is obtainable from the plant in correctly folded, preferably soluble form without a need for denaturation and renaturation. This plant-produced polypeptide is immunogenic without a need for exogenous adjuvants or other immunostimulatory materials. The polypeptide is preferably an scFv mol. that bears the idiotype of the surface Ig of a non-Hodgkin's (or B cell) lymphoma. Upon administration to a subject with lymphoma, the plant-produced, tumor-unique scFv polypeptide induces an idiotype-specific antibody or cell-mediated immune response against the lymphoma.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2001:247476 CAPLUS
 DOCUMENT NUMBER: 134:276460
 TITLE: Oligonucleotides of variable length and sequence for use as **linker** regions for dual-domain or multi-domain molecules
 INVENTOR(S): Reinl, Stephen J.; Lindbo, John A.; Turpen, Thomas
 PATENT ASSIGNEE(S): Large Scale Biology Corporation, USA
 SOURCE: PCT Int. Appl., 77 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2001023543 | A1 | 20010405 | WO 2000-US25965 | 20000922 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, | | | | |

KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2385609 AA 20010405 CA 2000-2385609 20000922
 EP 1218501 A1 20020703 EP 2000-965277 20000922
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL
 JP 2003510073 T2 20030318 JP 2001-526926 20000922
 ZA 2002002066 A 20030313 ZA 2002-2066 20020313
 US 1999-155978P P 19990924
 WO 2000-US25965 W 20000922
 PRIORITY APPLN. INFO.:

AB Disclosed are methods and compns. for creating a DNA, RNA or protein mol. with two or more nucleic acid or polypeptide domains, resp., joined by a **linker** region. These methods are used to generate random **linker** libraries of nucleic acids that encode dual-domain or multi-domain polypeptides. The **linker** regions are characterized by both length and sequence variability but may be made of repeats of a triplet sequence. Rules for the generation of the triplets for use in the linkers are given. The **linker** oligonucleotides may also be selected to bind to a specific protein. The linkers can be incorporated into nucleic acids of interest by PCR and these can then be ligated via the **linker** domains. Methods for ligating these amplification products and the removal of artifacts such as hybridization bubbles are described. Use of these linkers to construct a gene for a single chain antibody and expression of the gene in transgenic tobacco are demonstrated.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

| | | | |
|--|-------|------------|---------|
| => FIL STNGUIDE | | SINCE FILE | TOTAL |
| COST IN U.S. DOLLARS | | ENTRY | SESSION |
| FULL ESTIMATED COST | 22.82 | | 23.03 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | | SINCE FILE | TOTAL |
| CA SUBSCRIBER PRICE | -1.46 | ENTRY | SESSION |

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FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Feb 18, 2005 (20050218/UP).

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 19:55:58 ON 23 FEB 2005

| | |
|----|--------------------------------------|
| L1 | E REINL STEPHEN?/AU |
| 16 | E1 OR E2 |
| L2 | 6 L1 AND LINKER |
| L3 | 13 DUP REM L1 (3 DUPLICATES REMOVED) |
| L4 | 4 L3 AND LINKER |

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=> l3 not 14

L3 CANNOT BE SEARCHED IN STNGUIDE

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Enter DISPLAY HISTORY to see the sequence of commands that created
this L-number.

=> fil medline biosis caplus embase wpids

COST IN U.S. DOLLARS

SINCE FILE
ENTRY

TOTAL
SESSION

FULL ESTIMATED COST

0.96

23.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY

TOTAL
SESSION

CA SUBSCRIBER PRICE

0.00

-1.46

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=> l3 not 14

L5 9 L3 NOT L4

=> t ti 15 1-9

L5 ANSWER 1 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI Production of peptides in plants as viral coat protein fusions.

L5 ANSWER 2 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI Production of peptides in plants as viral coat protein fusions.

L5 ANSWER 3 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI Tobamovirus vectors for expression of recombinant genes in plants.

L5 ANSWER 4 OF 9 CPLUS COPYRIGHT 2005 ACS on STN
TI Secretory manufacture of heterooligomeric proteins using transgenic plant
expression hosts

L5 ANSWER 5 OF 9 CPLUS COPYRIGHT 2005 ACS on STN
TI Tobamovirus vectors for expression of recombinant genes in plants

L5 ANSWER 6 OF 9 CPLUS COPYRIGHT 2005 ACS on STN
TI Recombinant antigen fusion products with plant virus coat proteins
production in plant and parasite vaccine development

L5 ANSWER 7 OF 9 CPLUS COPYRIGHT 2005 ACS on STN
TI Malarial epitopes expressed on the surface of recombinant tobacco mosaic
virus

L5 ANSWER 8 OF 9 CPLUS COPYRIGHT 2005 ACS on STN
TI RAmy2A; a novel α -amylase-encoding gene in rice

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
TI Structural organization and differential expression of rice
α-amylase genes

=> d ibib abs 15 4

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:308513 CAPLUS
DOCUMENT NUMBER: 140:333557
TITLE: Secretory manufacture of heterooligomeric proteins
using transgenic plant expression hosts
INVENTOR(S): Reinl, Stephen J.; Edwards, Patricia
PATENT ASSIGNEE(S): Large Scale Biology Corporation, USA
SOURCE: PCT Int. Appl., 244 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004031362 | A2 | 20040415 | WO 2003-US31420 | 20031003 |
| WO 2004031362 | C1 | 20040610 | | |
| WO 2004031362 | A3 | 20041202 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004110930 | A1 | 20040610 | US 2003-679620 | 20031003 |
| PRIORITY APPLN. INFO.: | | | US 2002-415940P | P 20021003 |

AB A method of manufacturing heterooligomeric proteins in transgenic plants by
manufacturing them as a fusion protein containing a signal peptide and linked
by a peptide that can be used to direct accurate processing of the fusion
protein to independent subunits. The method is particularly intended for
use in the manufacture of IgGs and uses only a single transformation event to
obtain a suitable plant rather than the construction of separate plants
expressing heavy or light chain genes and crossing them to obtain a hybrid
producer plant. The propeptide linking the moieties of the fusion protein
may include a mol. chaperone that can direct folding of the protein to
ensure accurate processing. The use of the *Ustilago maydis* KP6 killer
toxin in the manufacture of monoclonal antibodies in transgenic tobacco is
demonstrated.

=> d his

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 19:55:58 ON 23
FEB 2005

E REINL STEPHEN?/AU

L1 16 E1 OR E2

L2 6 L1 AND LINKER
L3 13 DUP REM L1 (3 DUPLICATES REMOVED)
L4 4 L3 AND LINKER

FILE 'STNGUIDE' ENTERED AT 19:59:13 ON 23 FEB 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 20:08:39 ON 23
FEB 2005

L5 9 L3 NOT L4

=> logoff hold

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 20.32 | 44.31 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| CA SUBSCRIBER PRICE | -0.73 | -2.19 |

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 20:16:06 ON 23 FEB 2005

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1639MLS

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *

SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS'
AT 21:11:55 ON 23 FEB 2005

FILE 'MEDLINE' ENTERED AT 21:11:55 ON 23 FEB 2005

FILE 'BIOSIS' ENTERED AT 21:11:55 ON 23 FEB 2005

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FILE 'EMBASE' ENTERED AT 21:11:55 ON 23 FEB 2005

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FILE 'WPIDS' ENTERED AT 21:11:55 ON 23 FEB 2005

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 20.32 | 44.31 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| CA SUBSCRIBER PRICE | -0.73 | -2.19 |

=> fil medline biosis caplus embase wpids

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 20.32 | 44.31 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| CA SUBSCRIBER PRICE | -0.73 | -2.19 |

FILE 'MEDLINE' ENTERED AT 21:12:14 ON 23 FEB 2005

FILE 'BIOSIS' ENTERED AT 21:12:14 ON 23 FEB 2005
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FILE 'CAPLUS' ENTERED AT 21:12:14 ON 23 FEB 2005
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FILE 'EMBASE' ENTERED AT 21:12:14 ON 23 FEB 2005
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FILE 'WPIDS' ENTERED AT 21:12:14 ON 23 FEB 2005
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=> library and degenerate and linker and triplet and repeat?
L6 6 LIBRARY AND DEGENERATE AND LINKER AND TRIPLET AND REPEAT?

=> dup rem 16
PROCESSING COMPLETED FOR L6
L7 6 DUP REM L6 (0 DUPLICATES REMOVED)

=> t ti 17 1-6

L7 ANSWER 1 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Novel polypeptide self-antigen useful as tumor-specific vaccine in mammals, is produced in plants and mimics one or more epitopes of antigen uniquely expressed by cells of tumor.

L7 ANSWER 2 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Novel polypeptide self-antigen useful as tumor-specific vaccine in mammals, is produced in plants and mimics one or more epitopes of antigen uniquely expressed by cells of tumor.

L7 ANSWER 3 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Novel polypeptide antigen which includes epitope overexpressed by tumor cells e.g. B-cell lymphoma, and is capable of inducing immune response in mammal without need for adjuvant, useful as anti-tumor vaccine component.

L7 ANSWER 4 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Use of a polypeptide self-antigen as a tumor-specific vaccine.

L7 ANSWER 5 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Novel polypeptide vaccine produced in plants, useful for inducing an immune response to a self-antigen on the surface of certain tumor cells.

L7 ANSWER 6 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Novel **library** of dual-domain nucleic acid molecules useful for producing dual-domain proteins, or idiotypic scFv vaccine useful for treating B-cell lymphoma.

=> d his

(FILE 'HOME' ENTERED AT 19:55:41 ON 23 FEB 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 19:55:58 ON 23 FEB 2005

E REINL STEPHEN?/AU
L1 16 E1 OR E2
L2 6 L1 AND LINKER
L3 13 DUP REM L1 (3 DUPLICATES REMOVED)
L4 4 L3 AND LINKER

FILE 'STNGUIDE' ENTERED AT 19:59:13 ON 23 FEB 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 20:08:39 ON 23 FEB 2005

L5 9 L3 NOT L4

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 21:12:14 ON 23 FEB 2005

L6 6 LIBRARY AND DEGENERATE AND LINKER AND TRIPLET AND REPEAT?
L7 6 DUP REM L6 (0 DUPLICATES REMOVED)

=> 17 not 11

L8 6 L7 NOT L1

=> d ibib abs 17 2-6

L7 ANSWER 2 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-456551 [43] WPIDS
CROSS REFERENCE: 2001-596903 [67]; 2003-456552 [43]; 2003-492106 [46];
2003-492153 [46]
DOC. NO. CPI: C2003-121383

TITLE: Novel polypeptide self-antigen useful as tumor-specific vaccine in mammals, is produced in plants and mimics one or more epitopes of antigen uniquely expressed by cells of tumor.
 DERWENT CLASS: B04 D16
 INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H;
 TUSE, D
 PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I)
 REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D
 COUNTRY COUNT: 1
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|------|----------|-----------|----|----|
| US 2003044417 | A1 | 20030306 | (200343)* | | 37 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|----------------|-----------------------------------|----------------------|
| US 2003044417 | A1 Provisional | US 1999-155979P
US 2000-539382 | 19990924
20000331 |

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US
2000-539382 20000331

AN 2003-456551 [43] WPIDS
 CR 2001-596903 [67]; 2003-456552 [43]; 2003-492106 [46]; 2003-492153 [46]
 AB US2003044417 A UPAB: 20030928

NOVELTY - A polypeptide self-antigen (I) useful as a tumor- specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded by a nucleic acid (NA) in the cells of the tumor, including an epitope to, or overexpressed by tumor cells; produced in a cell or organism that has been transfected with NA and in a correctly folded form; and capable of inducing an immune response in a mammal, is new.

DETAILED DESCRIPTION - (I) is useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, which polypeptide:

(1) includes an epitope or epitopes unique to, or overexpressed by, cells of the tumor, thus distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(2) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(3) is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form;

(4) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

(1) an individual-specific immunogenic product (II) comprising (I), produced by a method which involves joining a nucleic acid encoding the first domain of the polypeptide to a nucleic acid encoding a first part of a **linker** to produce a first nucleic acid construct, joining the nucleic acid encoding a second part of the **linker** to a nucleic acid encoding the second domain of the polypeptide to produce a second nucleic acid construct, incorporating the first and the second constructs into a transient plant expression vector in frame so that, when expressed, the polypeptide bears the first and second domain separated by the **linker**, transfecting a plant with the vector so that the plant

temporarily produces the polypeptide, and recovering the polypeptide as a soluble, correctly-folded protein;

(2) a vaccine composition (III) useful for inducing a tumor specific immune response, idiotype-specific anti-lymphoma immune response, and polyclonal immune response to an idiotype of a surface immunoglobulin or to an idiotype in a mouse, comprising (I), and a pharmaceutical carrier or excipient; and

(3) production of (I).

ACTIVITY - Anti-tumor; Cytostatic.

MECHANISM OF ACTION - Vaccine (claimed); Inducer of immune response.

Treatment of lymphoma patient with the scFv polypeptide vaccine was demonstrated as follows. An idiotype-bearing scFv was produced from lymphoma cells of a human subject (designated JJ). JJ was subjected to immunization, and JJ's response was evaluated by laboratory tests and clinical observation. JJ's serum contained antibodies specific for the vaccine immunogen and reactive with a monoclonal Ig (that corresponded to the idiotypic lymphoma surface Ig). The antibodies were detected in an enzyme linked immunosorbent assay (ELISA) and by fluorescence activated cell sorter (FACS) analysis using cryopreserved lymphoma cells from JJ. JJ's peripheral blood T lymphocytes responded significantly in vitro to the vaccine polypeptide (or to the lymphoma cells as stimulators) by proliferation, measured as 3H-thymidine incorporation and by secretion of interferon-gamma. JJ's peripheral blood mononuclear cells also produced TNF alpha in response to these stimuli. JJ's clinical response was characterized by radiographic evidence of lack of tumor progression and gradual disappearance of the lymphoma. No radiographic or other clinical signs of relapse were evident over one year of observation.

USE - (I) is useful as a tumor-specific vaccine, especially a B-cell lymphoma-specific vaccine. (III) is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject, preferably human or a subject who had a tumor and was treated so that no tumor is clinically or radiographically evident, where the tumor is B-cell lymphoma (claimed).

Dwg.0/5

L7 ANSWER 3 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-492153 [46] WPIDS
CROSS REFERENCE: 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43];
2003-492106 [46]
DOC. NO. NON-CPI: N2003-390915
DOC. NO. CPI: C2003-131636
TITLE: Novel polypeptide antigen which includes epitope overexpressed by tumor cells e.g. B-cell lymphoma, and is capable of inducing immune response in mammal without need for adjuvant, useful as anti-tumor vaccine component.
DERWENT CLASS: B04 D16 P13
INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H;
TUSE, D
PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I)
REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|------|----------|-----------|----|----|
| US 2003039659 | A1 | 20030227 | (200346)* | | 48 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|----------------|-----------------|----------|
| US 2003039659 | A1 Provisional | US 1999-155979P | 19990924 |

Div ex

US 2000-522900
US 2002-67892

20000310
20020208

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US
2000-522900 20000310; US
2002-67892 20020208

AN 2003-492153 [46] WPIDS

CR 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46]

AB US2003039659 A UPAB: 20030719

NOVELTY - A polypeptide self-antigen (I) useful as tumor- specific vaccine in subject with a tumor, including an epitope or epitope unique to, or overexpressed by, cells of the tumor, is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from tumor of subject, and is capable of inducing an immune response in a mammal without a need for adjuvant or other immunostimulatory materials, is new.

DETAILED DESCRIPTION - A polypeptide self-antigen (I) useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, is new. The polypeptide:

(a) includes an epitope or epitope unique to, or overexpressed by, cells of the tumor, thus distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(b) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(c) is obtainable from the cell or organism in correctly folder from, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form; or

(d) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

(1) an individual-specific immunogenic product (II) comprising (I) produced transiently in a plant, and which is a 2-domain scFv antibody that includes part of variable heavy (VH) and variable light (VL) domains and are linked by an amino acid **linker**, comprising:

(a) joining a nucleic acid encoding the first domain of the polypeptide to a nucleic acid encoding a first part of a **linker** to produce a first nucleic acid construct;

(b) joining the nucleic acid encoding a second part of the **linker** to a nucleic acid encoding the second domain of the polypeptide to produce a second nucleic acid construct;

(c) incorporating the first and second constructs into a transient plant expression vector in frame so that, when expressed, the polypeptide bears the first and second domain separated by the **linker**, transfecing a plant with the vector so that the plant transiently produces the polypeptide; and

(d) recovering the polypeptide as a soluble, correctly-folded protein;

(2) a vaccine composition (III) useful for inducing a tumor specific immune response, e.g. a idiotype-specific anti-lymphoma immune response, comprising (I) produced transiently in a plant, and which is a 2-domain scFv antibody that includes part of VH and VL domains and are linked by an amino acid **linker**, and a carrier or excipient;

(3) a vaccine composition (IV) useful for inducing a polyclonal immune response to an idiotype in a mouse comprising (II) and a carrier or excipient; and

(4) producing (I).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Inducer of protective anti-tumor immune response (cellular, humoral or both) in a mammal; Vaccine.

An idiotype-bearing scFv was produced from lymphoma cells of a human subject (designated JJ) using mRNA from the lymphoma cells to make cDNA which is PCR amplified using appropriate primers to amplify the VH and VL coding sequences. This DNA was expressed in a Nicotiana benthamiana plant by cloning into modified tobamoviral vector using the random **linker library** approach. The scFv corresponding to JJ's lymphoma surface Ig idiotype was obtained from the plants and formulated into a vaccine. The vaccine was administered by successive SC injections of 0.5 mg of the antigen. JJ's response was evaluated by laboratory tests and clinical observation. The following results were obtained. JJ's serum contained antibodies specific for the vaccine immunogen and reactive with a monoclonal Ig (that corresponds to the idiotypic lymphoma surface Ig). JJ's peripheral blood T lymphocytes responded significantly in vitro to the vaccine polypeptide (or to the lymphoma cells as stimulators) by proliferation, measured as 3H-thymidine incorporation and by secretion of interferon- gamma . JJ's peripheral blood mononuclear cells also produce tumor necrosis factor (TNF)- alpha in response to these stimuli. JJ's clinical response was characterized by radiographic evidence of lack of tumor progression and gradual disappearance of the lymphoma.

USE - (I) is useful for inducing an immune response, preferably a protective anti-tumor immune response in a mammal, preferably human. (III) is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject (preferably human) or a subject who had a tumor and was treated so that no tumor is clinically radiographically evident. (III) comprises the polypeptide in unit dosage form in aqueous solution at a concentration of 0.1-10 mg/ml. The vaccines are preferably useful for inducing immune antibody response against B-cell lymphoma. (All claimed.)

ADVANTAGE - The polypeptide is produced without the need for denaturation or renaturation. (I) is rapidly produced in plants by transient viral expression. Plant samples expressing the desired protein can be positively identified by both enzyme linked immunosorbent assay (ELISA) and Western blotting 4 weeks after molecular cloning. Thus, (I) is expressed rapidly and easily in plants.

Dwg.0/5

L7 ANSWER 4 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-492106 [46] WPIDS
CROSS REFERENCE: 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43];
2003-492153 [46]
DOC. NO. NON-CPI: N2003-390889
DOC. NO. CPI: C2003-131600
TITLE: Use of a polypeptide self-antigen as a tumor-specific vaccine.
DERWENT CLASS: B04 D16 P13
INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H;
TUSE, D
PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I)
REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|------|----------|-----------|----|----|
| US 2003035807 | A1 | 20030220 | (200346)* | | 47 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|----------------|-----------------|----------|
| US 2003035807 | A1 Provisional | US 1999-155979P | 19990924 |

| | | |
|--------|----------------|----------|
| Div ex | US 2000-522900 | 20000310 |
| | US 2002-67790 | 20020208 |

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US
2000-522900 20000310; US
2002-67790 20020208

AN 2003-492106 [46] WPIDS
CR 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43]; 2003-492153 [46]
AB US2003035807 A UPAB: 20030719

NOVELTY - A polypeptide self-antigen useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor and is encoded at least in part by a nucleic acid in the cells of the tumor, is new.

DETAILED DESCRIPTION - The polypeptide:

(a) includes an epitope or epitopes unique to, or overexpressed by, cells of the tumor, for distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(b) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(c) is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form;

(d) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitopes.

INDEPENDENT CLAIMS are also included for:

(1) an individual-specific immunogenic product comprising the polypeptide;
(2) a vaccine composition;
(3) inducing a tumor-specific immune antibody response in a tumor-bearing subject or a subject who had a tumor and was treated so that no tumor is clinically or radiographically evident; and
(4) producing the polypeptide.

ACTIVITY - Cytostatic.

No suitable data given.

MECHANISM OF ACTION - Gene therapy; Vaccine.

USE - The polypeptide self antigen is useful for treating or preventing tumor.

Dwg.0/5

L7 ANSWER 5 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-596903 [67] WPIDS
CROSS REFERENCE: 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46];
2003-492153 [46]
DOC. NO. CPI: C2001-176650
TITLE: Novel polypeptide vaccine produced in plants, useful for inducing an immune response to a self-antigen on the surface of certain tumor cells.
DERWENT CLASS: B04 D16
INVENTOR(S): REINL, S J; TURPEN, T H; LINDBO, J A; MCCORMICK, A A;
TUSE, D
PATENT ASSIGNEE(S): (LARG-N) LARGE SCALE BIOLOGY CORP; (MCCO-I) MCCORMICK A
A; (TUSE-I) TUSE D
COUNTRY COUNT: 95
PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LA | PG |
|---|--------------------------|------|----|----|
| WO 2001068682 | A1 20010920 (200167)* EN | 89 | | |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ | | | | |

NL OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
 AU 2001012019 A 20010924 (200208)
 EP 1263779 A1 20021211 (200301) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 JP 2003527399 W 20030916 (200362) 117
 ZA 2002006798 A 20031126 (200402) 94
 EP 1263779 B1 20041215 (200482) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
 DE 60016806 E 20050120 (200510)

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|------------------|----------|
| WO 2001068682 | A1 | WO 2000-US28362 | 20001013 |
| AU 2001012019 | A | AU 2001-12019 | 20001013 |
| EP 1263779 | A1 | EP 2000-973516 | 20001013 |
| | | WO 2000-US28362 | 20001013 |
| JP 2003527399 | W | WO 2000-US28362 | 20001013 |
| | | JP 2001-567772 | 20001013 |
| ZA 2002006798 | A | ZA 2002-6798 | 20020826 |
| EP 1263779 | B1 | EP 2000-973516 | 20001013 |
| | | WO 2000-US28362 | 20001013 |
| DE 60016806 | E | DE 2000-00016806 | 20001013 |
| | | EP 2000-973516 | 20001013 |
| | | WO 2000-US28362 | 20001013 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|---------------|
| AU 2001012019 | A Based on | WO 2001068682 |
| EP 1263779 | A1 Based on | WO 2001068682 |
| JP 2003527399 | W Based on | WO 2001068682 |
| EP 1263779 | B1 Based on | WO 2001068682 |
| DE 60016806 | E Based on | EP 1263779 |
| | Based on | WO 2001068682 |

PRIORITY APPLN. INFO: US 2000-522900 20000310
 AN 2001-596903 [67] WPIDS
 CR 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46]; 2003-492153 [46]
 AB WO 200168682 A UPAB: 20050211

NOVELTY - A polypeptide self-antigen (I) useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, is new.

DETAILED DESCRIPTION - (I) includes an epitope or epitopes unique to, or over expressed by, cells of the tumor, thereby distinguishing the tumor from all other tumors of the same or different histological type, or in the subject or in another member of the subject's species. (I) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject, is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form. (I) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or

cell-mediated response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

- (1) an individual-specific immunogenic product (II) comprising (I);
- (2) a vaccine composition (VC) useful for inducing a tumor-specific immune response, idiotype-specific anti-lymphoma immune response, a polyclonal immune response to at least one idiotype of a surface immunoglobulin or a polyclonal immune response to an idiotype in a mouse, comprising (I); and
- (3) producing (I).

ACTIVITY - Cytostatic; immunostimulator. The idiotype-bearing self antigen was administered by successive subcutaneous injection of 0.5 mg of the antigen and ISAF-1 adjuvant to humans with low grade B-cell lymphoma. The patients were given additional injections once a month for 5 months and booster doses were given annually. The results indicated that at least 6 of the 20 patients showed both immunological and clinical, including radiographic, signs of therapeutic success. The sera had significant titers of antibodies specific for the idiotype of their lymphoma cells and ScFv polypeptide used for immunization. Clinically, no signs of tumor progression and a statistically significant prolonged disease free interval after vaccination compared to historical controls, were observed. PCR (polymerase chain reaction) analysis of lymphocyte DNA across bcl-2/Igh, a molecular marker of human lymphoma, further confirmed the successful treatment of the lymphoma.

MECHANISM OF ACTION - Polyclonal anti-idiotypic antibody response inducer; cell-mediated immune response inducer (claimed).

USE - VC is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject or a subject who had a tumor e.g. B-cell lymphoma, and was treated so that no tumor is clinically or radiographically evident. (I) is useful for inducing a protective antitumor immune response (claimed).

ADVANTAGE - (I) can be produced at high levels, easy to purify and can be appropriately folded to mimic the conformation of the native epitopes displayed at the tumor cell surface.

Dwg.0/5

L7 ANSWER 6 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-316135 [33] WPIDS
DOC. NO. CPI: C2001-097326
TITLE: Novel **library** of dual-domain nucleic acid molecules useful for producing dual-domain proteins, or idiotypic scFv vaccine useful for treating B-cell lymphoma.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): LINDBO, J A; REINL, S J; TURPEN, T; REINL, S
PATENT ASSIGNEE(S): (LARG-N) LARGE SCALE BIOLOGY CORP
COUNTRY COUNT: 91
PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LA | PG |
|---------------|--|------|----|----|
| ----- | | | | |
| WO 2001023543 | A1 20010405 (200133)* | EN | 77 | |
| RW: | AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW | | | |
| W: | AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW | | | |
| AU 2000076017 | A 20010430 (200142) | | | |
| EP 1218501 | A1 20020703 (200251) | EN | | |
| R: | AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI | | | |
| KR 2002059413 | A 20020712 (200306) | | | |

JP 2003510073 W 20030318 (200321) 103
 ZA 2002002066 A 20030528 (200341) 82

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|-----------------|----------|
| WO 2001023543 | A1 | WO 2000-US25965 | 20000922 |
| AU 2000076017 | A | AU 2000-76017 | 20000922 |
| EP 1218501 | A1 | EP 2000-965277 | 20000922 |
| | | WO 2000-US25965 | 20000922 |
| KR 2002059413 | A | KR 2002-703842 | 20020323 |
| JP 2003510073 | W | WO 2000-US25965 | 20000922 |
| | | JP 2001-526926 | 20000922 |
| ZA 2002002066 | A | ZA 2002-2066 | 20020313 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|---------------|
| AU 2000076017 | A Based on | WO 2001023543 |
| EP 1218501 | A1 Based on | WO 2001023543 |
| JP 2003510073 | W Based on | WO 2001023543 |

PRIORITY APPLN. INFO: US 1999-155978P 19990924

AN 2001-316135 [33] WPIDS

AB WO 200123543 A UPAB: 20010615

NOVELTY - A **library** (I) of dual-domain nucleic acid molecules, each having a first and a second domain that are separated and linked by a **linker** which is a member of a randomized **library** (RL) of linkers that vary in size and nucleotide sequence and consists of a **repeated pattern** (RP) of **degenerate repeated triplet** nucleotides, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a dual-domain nucleic acid molecule (II) selected from (I);
- (2) a **library** (III) of dual-domain polypeptide molecules each described by the formula D1-L-D2, where D1 and D2 are polypeptide domains and L is a peptide or a polypeptide **linker** which is a member of RL;
- (3) a **library** (IV) of multi-domain polypeptide molecules each comprising polypeptide domains D each pair of which is linked by a peptide or polypeptide **linker** L, each molecule being described by the formula DxLy, where x = 2-20 and y = 1-19, with the condition that for any value of x:
 - (i) y = x-1;
 - (ii) D1 is bonded to a single C-terminal **linker**;
 - (iii) the C-terminal-most D is bonded to a single N-terminal **linker**;
 - (iv) each of D2-D19 are bonded to a N-terminal and a C-terminal **linker**; and
 - (v) each L is a member of RL;
- (4) a dual-domain polypeptide molecule (V) selected from (III);
- (5) a multi-domain polypeptide molecule (VI) selected from (IV);
- (6) generating (I);
- (7) a population of dual-domain polypeptides (VIII) or a dual-domain polypeptide of the population, obtained by the above method;
- (8) producing (V);
- (9) a **linker** nucleic acid molecule or a sequence (IX) that joins two nucleic acid domains or two nucleic acid sequences encoding two polypeptide domains, which has a pattern of **degenerate repeated triplet** nucleotides, where all the three

nucleotides at positions 1-3 are different, and the molecule or sequence that joins the domains does not encode Gly4Ser or its **repeat**;

- (10) a **library** (X) of (IX); and
- (11) making (X).

USE - (I) is useful for producing dual-domain proteins of interest that have therapeutic value, e.g., idiotypic scFv vaccine for treating B-cell lymphoma.

ADVANTAGE - The expression systems obtained by the above said methods are suitable for rapid and economical production of useful quantities of correctly folded polypeptides in surprisingly high abundance and potent immunogenicity.

Dwg.0/3

=> degenerate and linker and triplet and repeat?

L9 6 DEGENERATE AND LINKER AND TRIPLET AND REPEAT?

=> 19 not 17

L10 0 L9 NOT L7

=> library and linker and triplet and repeat?

L11 8 LIBRARY AND LINKER AND TRIPLET AND REPEAT?

=> l11 not 19

L12 2 L11 NOT L9

=> t ti l12 1-2

L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

TI Oligonucleotides of variable length and sequence for use as **linker** regions for dual-domain or multi-domain molecules

L12 ANSWER 2 OF 2 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI New composite binding zinc finger polypeptide, useful for designing sequence-specific binding proteins regulating gene expression in the fields of molecular biology, and for the diagnosis and treatment of autoimmune disorders.

=> d ibib abs l12 1-2

L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:247476 CAPLUS

DOCUMENT NUMBER: 134:276460

TITLE: Oligonucleotides of variable length and sequence for use as **linker** regions for dual-domain or multi-domain molecules

INVENTOR(S): Reinl, Stephen J.; Lindbo, John A.; Turpen, Thomas

PATENT ASSIGNEE(S): Large Scale Biology Corporation, USA

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2001023543 | A1 | 20010405 | WO 2000-US25965 | 20000922 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, | | | | |

MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
 SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2385609 AA 20010405 CA 2000-2385609 20000922
 EP 1218501 A1 20020703 EP 2000-965277 20000922
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL
 JP 2003510073 T2 20030318 JP 2001-526926 20000922
 ZA 2002002066 A 20030313 ZA 2002-2066 20020313
 PRIORITY APPLN. INFO.: US 1999-155978P P 19990924
 WO 2000-US25965 W 20000922

AB Disclosed are methods and compns. for creating a DNA, RNA or protein mol. with two or more nucleic acid or polypeptide domains, resp., joined by a **linker** region. These methods are used to generate random **linker** libraries of nucleic acids that encode dual-domain or multi-domain polypeptides. The **linker** regions are characterized by both length and sequence variability but may be made of **repeats** of a **triplet** sequence. Rules for the generation of the triplets for use in the linkers are given. The **linker** oligonucleotides may also be selected to bind to a specific protein. The linkers can be incorporated into nucleic acids of interest by PCR and these can then be ligated via the **linker** domains. Methods for ligating these amplification products and the removal of artifacts such as hybridization bubbles are described. Use of these linkers to construct a gene for a single chain antibody and expression of the gene in transgenic tobacco are demonstrated.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 2 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2003-278214 [27] WPIDS
 DOC. NO. NON-CPI: N2003-221052
 DOC. NO. CPI: C2003-072580
 TITLE: New composite binding zinc finger polypeptide, useful for designing sequence-specific binding proteins regulating gene expression in the fields of molecular biology, and for the diagnosis and treatment of autoimmune disorders.
 DERWENT CLASS: B04 D16 T01
 INVENTOR(S): CHOO, Y; ISALAN, M; MOORE, M; SEPP, A
 PATENT ASSIGNEE(S): (SANG-N) SANGAMO BIOSCIENCES INC; (CHOO-I) CHOO Y;
 (ISAL-I) ISALAN M; (MOOR-I) MOORE M; (SEPP-I) SEPP A
 COUNTRY COUNT: 97
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|---|--------------------|------|-----|----|
| WO 2002099084 | A2 | 20021212 (200327)* | EN | 157 | |
| RW: | AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ | | | | |
| | NL OA PT SD SE SL SZ TR TZ UG ZM ZW | | | | |
| W: | AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK | | | | |
| | DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR | | | | |
| | KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU | | | | |
| | SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW | | | | |
| AU 2002322477 | A1 | 20021216 (200452) | | | |
| US 2004197892 | A1 | 20041007 (200466) | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-----------|------|-------------|------|
|-----------|------|-------------|------|

| | | | |
|---------------|----|-----------------|----------|
| WO 2002099084 | A2 | WO 2002-US22272 | 20020404 |
| AU 2002322477 | A1 | AU 2002-322477 | 20020404 |
| US 2004197892 | A1 | WO 2002-US22272 | 20020404 |

US 2004-474282 20040426

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|---------------|
| AU 2002322477 | A1 Based on | WO 2002099084 |

PRIORITY APPLN. INFO: GB 2001-8491 20010404

AN 2003-278214 [27] WPIDS

AB WO 200299084 A UPAB: 20030429

NOVELTY - A new composite binding polypeptide comprises a first natural binding domain derived from a first natural binding polypeptide, and a second natural binding domain derived from a second natural binding polypeptide, where the first and second natural binding polypeptides may be the same or different, and where the polypeptide binds to a target differing from the natural target of both the first and second binding polypeptides.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (a) a chimeric polypeptide comprising a binding polypeptide cited above, and a biological effector domain;
- (b) a **library** of natural binding domains;
- (c) a **library** of natural zinc finger nucleic acid binding domains comprising a **linker** attached to it;
- (d) a method for selecting a binding polypeptide capable of binding to a target site, comprising providing a **library** of natural binding domain, assembling two or more of the domains to form a composite polypeptide, and screening the composite polypeptide against the target site in order to determine its ability to bind the target site;
- (e) a method for designing a composite binding polypeptide, comprising providing information defining a target site, selecting, from a database of natural binding domains, sequences of binding domains which are predicted to bind to the target site by the application of one or more rules which define target binding interactions for the binding domains, and displaying the sequences of the binding domains, separated by **linker** sequences, and optionally assembling the binding polypeptide from a **library** of the domains; and
- (f) a computer-implemented method for designing a zinc finger polypeptide.

ACTIVITY - Immunosuppressive. No biological data given.

MECHANISM OF ACTION - Gene-Therapy; Zinc-Finger-Protein-agonist; Zinc-Finger-Protein-Antagonist.

USE - The methods and compositions of the present invention are useful for designing sequence-specific binding proteins for regulation of gene expression in the fields of molecular biology. They can also be used in the diagnosis and treatment of autoimmune disorders, and as research tools and in transgenic animals.

Dwg.0/6

=> linker and triplet and repeat?

L13 38 LINKER AND TRIPLET AND REPEAT?

=> dup rem 113

PROCESSING COMPLETED FOR L13

L14 18 DUP REM L13 (20 DUPLICATES REMOVED)

=> d his

(FILE 'HOME' ENTERED AT 19:55:41 ON 23 FEB 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 19:55:58 ON 23 FEB 2005

E REINL STEPHEN?/AU

L1 16 E1 OR E2
L2 6 L1 AND LINKER
L3 13 DUP REM L1 (3 DUPLICATES REMOVED)
L4 4 L3 AND LINKER

FILE 'STNGUIDE' ENTERED AT 19:59:13 ON 23 FEB 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 20:08:39 ON 23 FEB 2005

L5 9 L3 NOT L4

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 21:12:14 ON 23 FEB 2005

L6 6 LIBRARY AND DEGENERATE AND LINKER AND TRIPLET AND REPEAT?
L7 6 DUP REM L6 (0 DUPLICATES REMOVED)
L8 6 L7 NOT L1
L9 6 DEGENERATE AND LINKER AND TRIPLET AND REPEAT?
L10 0 L9 NOT L7
L11 8 LIBRARY AND LINKER AND TRIPLET AND REPEAT?
L12 2 L11 NOT L9
L13 38 LINKER AND TRIPLET AND REPEAT?
L14 18 DUP REM L13 (20 DUPLICATES REMOVED)

=> l14 not 19

L15 14 L14 NOT L9

=> l15 not 112

L16 12 L15 NOT L12

=> l16 not 13

L17 11 L16 NOT L3

=> l17 not 12

L18 11 L17 NOT L2

=> l18 not 16

L19 11 L18 NOT L6

=> t ti l19 1-11

L19 ANSWER 1 OF 11 MEDLINE on STN

TI Control of Hapl-DNA site recognition through the interplay of multiple distinct intermolecular interactions.

L19 ANSWER 2 OF 11 MEDLINE on STN

TI Novel oligosaccharide side chains of the collagen-like region of BclA, the major glycoprotein of the *Bacillus anthracis* exosprium.

L19 ANSWER 3 OF 11 MEDLINE on STN

TI Distance-dependent cellular palmitoylation of de-novo-designed sequences and their translocation to plasma membrane subdomains.

L19 ANSWER 4 OF 11 MEDLINE on STN

TI A signal encoded in vertebrate DNA that influences nucleosome positioning and alignment.

L19 ANSWER 5 OF 11 MEDLINE on STN
TI A **linker** region of the yeast zinc cluster protein leu3p specifies binding to everted **repeat** DNA.

L19 ANSWER 6 OF 11 MEDLINE on STN
TI 1H, 15N resonance assignment and three-dimensional structure of CYP1 (HAP1) DNA-binding domain.

L19 ANSWER 7 OF 11 MEDLINE on STN
TI Capillary electrophoresis of polymerase chain reaction-amplified products in polymer networks: the case of Kennedy's disease.

L19 ANSWER 8 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI A survey of TWIST for mutations in craniosynostosis reveals a variable length polyglycine tract in asymptomatic individuals.

L19 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
TI Structural characterization of the inhibitory DNA motif for the type A (D)-CpG-induced cytokine secretion and NK-cell lytic activity in mouse spleen cells

L19 ANSWER 10 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Antibacterial beta-peptide exhibiting antibacterial properties by producing cavities in membranes or by peptide induced leakage of liposomal content.

L19 ANSWER 11 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New antibacterial beta-peptide having antibacterial properties for use in materials for making surfaces, fibers and films such as medical devices, countertops, cutting boards, sponges, packaging materials and wipes.

=> d ibib abs 19 1-10

L9 ANSWER 1 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-492153 [46] WPIDS
CROSS REFERENCE: 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43];
2003-492106 [46]
DOC. NO. NON-CPI: N2003-390915
DOC. NO. CPI: C2003-131636
TITLE: Novel polypeptide antigen which includes epitope overexpressed by tumor cells e.g. B-cell lymphoma, and is capable of inducing immune response in mammal without need for adjuvant, useful as anti-tumor vaccine component.
DERWENT CLASS: B04 D16 P13
INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H;
TUSE, D
PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I)
REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LA | PG |
|---------------|-----------------------|------|----|----|
| US 2003039659 | A1 20030227 (200346)* | | 48 | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-----------|------|-------------|------|
|-----------|------|-------------|------|

US 2003039659 A1 Provisional US 1999-155979P 19990924
Div ex US 2000-522900 20000310
US 2002-67892 20020208

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US
2000-522900 20000310; US
2002-67892 20020208

AN 2003-492153 [46] WPIDS

CR 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46]

AB US2003039659 A UPAB: 20030719

NOVELTY - A polypeptide self-antigen (I) useful as tumor- specific vaccine in subject with a tumor, including an epitope or epitope unique to, or overexpressed by, cells of the tumor, is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from tumor of subject, and is capable of inducing an immune response in a mammal without a need for adjuvant or other immunostimulatory materials, is new.

DETAILED DESCRIPTION - A polypeptide self-antigen (I) useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, is new. The polypeptide:

(a) includes an epitope or epitope unique to, or overexpressed by, cells of the tumor, thus distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(b) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(c) is obtainable from the cell or organism in correctly folder from, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form; or

(d) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

(1) an individual-specific immunogenic product (II) comprising (I) produced transiently in a plant, and which is a 2-domain scFv antibody that includes part of variable heavy (VH) and variable light (VL) domains and are linked by an amino acid **linker**, comprising:

(a) joining a nucleic acid encoding the first domain of the polypeptide to a nucleic acid encoding a first part of a **linker** to produce a first nucleic acid construct;

(b) joining the nucleic acid encoding a second part of the **linker** to a nucleic acid encoding the second domain of the polypeptide to produce a second nucleic acid construct;

(c) incorporating the first and second constructs into a transient plant expression vector in frame so that, when expressed, the polypeptide bears the first and second domain separated by the **linker**, transfecing a plant with the vector so that the plant transiently produces the polypeptide; and

(d) recovering the polypeptide as a soluble, correctly-folded protein;

(2) a vaccine composition (III) useful for inducing a tumor specific immune response, e.g. a idiotype-specific anti-lymphoma immune response, comprising (I) produced transiently in a plant, and which is a 2-domain scFv antibody that includes part of VH and VL domains and are linked by an amino acid **linker**, and a carrier or excipient;

(3) a vaccine composition (IV) useful for inducing a polyclonal immune response to an idiotype in a mouse comprising (II) and a carrier or excipient; and

(4) producing (I).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Inducer of protective anti-tumor immune response (cellular, humoral or both) in a mammal; Vaccine.

An idiotype-bearing scFv was produced from lymphoma cells of a human subject (designated JJ) using mRNA from the lymphoma cells to make cDNA which is PCR amplified using appropriate primers to amplify the VH and VL coding sequences. This DNA was expressed in a Nicotiana benthamiana plant by cloning into modified tobamoviral vector using the random **linker** library approach. The scFv corresponding to JJ's lymphoma surface Ig idiotype was obtained from the plants and formulated into a vaccine. The vaccine was administered by successive SC injections of 0.5 mg of the antigen. JJ's response was evaluated by laboratory tests and clinical observation. The following results were obtained. JJ's serum contained antibodies specific for the vaccine immunogen and reactive with a monoclonal Ig (that corresponds to the idotypic lymphoma surface Ig). JJ's peripheral blood T lymphocytes responded significantly in vitro to the vaccine polypeptide (or to the lymphoma cells as stimulators) by proliferation, measured as 3H-thymidine incorporation and by secretion of interferon- gamma . JJ's peripheral blood mononuclear cells also produce tumor necrosis factor (TNF)- alpha in response to these stimuli. JJ's clinical response was characterized by radiographic evidence of lack of tumor progression and gradual disappearance of the lymphoma.

USE - (I) is useful for inducing an immune response, preferably a protective anti-tumor immune response in a mammal, preferably human. (III) is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject (preferably human) or a subject who had a tumor and was treated so that no tumor is clinically radiographically evident. (III) comprises the polypeptide in unit dosage form in aqueous solution at a concentration of 0.1-10 mg/ml. The vaccines are preferably useful for inducing immune antibody response against B-cell lymphoma. (All claimed.)

ADVANTAGE - The polypeptide is produced without the need for denaturation or renaturation. (I) is rapidly produced in plants by transient viral expression. Plant samples expressing the desired protein can be positively identified by both enzyme linked immunosorbent assay (ELISA) and Western blotting 4 weeks after molecular cloning. Thus, (I) is expressed rapidly and easily in plants.

Dwg.0/5

L9 ANSWER 2 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-492106 [46] WPIDS
CROSS REFERENCE: 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43];
2003-492153 [46]
DOC. NO. NON-CPI: N2003-390889
DOC. NO. CPI: C2003-131600
TITLE: Use of a polypeptide self-antigen as a tumor-specific vaccine.
DERWENT CLASS: B04 D16 P13
INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H;
TUSE, D
PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I)
REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LA | PG |
|---------------|-----------------------|------|----|----|
| US 2003035807 | A1 20030220 (200346)* | | 47 | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-----------|------|-------------|------|
|-----------|------|-------------|------|

US 2003035807 A1 Provisional US 1999-155979P 19990924
Div ex US 2000-522900 20000310
US 2002-67790 20020208

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US
2000-522900 20000310; US
2002-67790 20020208

AN 2003-492106 [46] WPIDS

CR 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43]; 2003-492153 [46]

AB US2003035807 A UPAB: 20030719

NOVELTY - A polypeptide self-antigen useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor and is encoded at least in part by a nucleic acid in the cells of the tumor, is new.

DETAILED DESCRIPTION - The polypeptide:

(a) includes an epitope or epitopes unique to, or overexpressed by, cells of the tumor, for distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(b) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(c) is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form;

(d) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitopes.

INDEPENDENT CLAIMS are also included for:

(1) an individual-specific immunogenic product comprising the polypeptide;

(2) a vaccine composition;

(3) inducing a tumor-specific immune antibody response in a tumor-bearing subject or a subject who had a tumor and was treated so that no tumor is clinically or radiographically evident; and

(4) producing the polypeptide.

ACTIVITY - Cytostatic.

No suitable data given.

MECHANISM OF ACTION - Gene therapy; Vaccine.

USE - The polypeptide self antigen is useful for treating or preventing tumor.

Dwg.0/5

L9 ANSWER 3 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-456552 [43] WPIDS

CROSS REFERENCE: 2001-596903 [67]; 2003-456551 [43]; 2003-492106 [46];
2003-492153 [46]

DOC. NO. CPI: C2003-121384

TITLE: Novel polypeptide self-antigen useful as tumor-specific vaccine in mammals, is produced in plants and mimics one or more epitopes of antigen uniquely expressed by cells of tumor.

DERWENT CLASS: B04 D16

INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H;
TUSE, D

PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I)
REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D

COUNTRY COUNT: 1

PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LA | PG |
|-----------|-----------|------|----|----|
|-----------|-----------|------|----|----|

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|----------------|-----------------|----------|
| US 2003044420 | A1 Provisional | US 1999-155979P | 19990924 |
| | Div ex | US 2000-522900 | 20000310 |
| | | US 2002-67893 | 20020208 |

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US
 2000-522900 20000310; US
 2002-67893 20020208

AN 2003-456552 [43] WPIDS

CR 2001-596903 [67]; 2003-456551 [43]; 2003-492106 [46]; 2003-492153 [46]

AB US2003044420 A UPAB: 20030928

NOVELTY - A polypeptide self-antigen (I) useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded by a nucleic acid (NA) in the cells of the tumor, including an epitope to, or overexpressed by tumor cells; produced in a cell or organism that has been transfected with NA and in a correctly folded form; and capable of inducing an immune response in a mammal, is new.

DETAILED DESCRIPTION - (I) is useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, which polypeptide:

(a) includes an epitope or epitopes unique to, or overexpressed by, cells of the tumor, so distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(b) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(c) is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form;

(d) is capable of including an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

(1) an individual-specific immunogenic product (II) comprising (I), produced by a method which involves joining a nucleic acid encoding the first domain of the polypeptide to a nucleic acid encoding a first part of a **linker** to produce a first nucleic acid construct, joining the nucleic acid encoding a second part of the **linker** to a nucleic acid encoding the second domain of the polypeptide to produce a second nucleic acid construct, incorporating the first and the second constructs into a transient plant expression vector in frame so that, when expressed, the polypeptide bears the first and second domain separated by the **linker**, transfecting a plant with the vector so that the plant transiently produces the polypeptide, and recovering the polypeptide as a soluble, correctly-folded protein;

(2) a vaccine composition (III) useful for inducing a tumor specific immune response, idiotype-specific anti-lymphoma immune response, and polyclonal immune response to an idiotype of a surface immunoglobulin or to an idiotype in a mouse, comprising (I), and a pharmaceutical carrier or excipient; and

(3) production of (I).

ACTIVITY - Anti-tumor; Cytostatic.

MECHANISM OF ACTION - Vaccine (claimed). Treatment of lymphoma patient with the scFv polypeptide vaccine was demonstrated as follows. An

idiotype-bearing scFv was produced from lymphoma cells of a human subject (designated JJ). JJ was subjected to immunization, and JJ's response was evaluated by laboratory tests and clinical observation. JJ's serum contained antibodies specific for the vaccine immunogen and reactive with a monoclonal Ig (that corresponded to the idiotypic lymphoma surface Ig). The antibodies were detected in an enzyme linked immunosorbent assay (ELISA) and by fluorescence activated cell sorter (FACS) analysis using cryopreserved lymphoma cells from JJ. JJ's peripheral blood T lymphocytes responded significantly in vitro to the vaccine polypeptide (or to the lymphoma cells as stimulators) by proliferation, measured as 3H-thymidine incorporation and by secretion of interferon-gamma. JJ's peripheral blood mononuclear cells also produced TNF alpha in response to these stimuli. JJ's clinical response was characterized by radiographic evidence of lack of tumor progression and gradual disappearance of the lymphoma. No radiographic or other clinical signs of relapse were evident over one year of observation.

USE - (I) is useful as a tumor-specific vaccine, especially a B-cell lymphoma-specific vaccine. (III) is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject, preferably human or a subject who had a tumor and was treated so that no tumor is clinically or radiographically evident, where the tumor is B-cell lymphoma (claimed).

Dwg.0/5

L9 ANSWER 4 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2003-456551 [43] WPIDS
 CROSS REFERENCE: 2001-596903 [67]; 2003-456552 [43]; 2003-492106 [46];
 2003-492153 [46]
 DOC. NO. CPI: C2003-121383
 TITLE: Novel polypeptide self-antigen useful as tumor-specific vaccine in mammals, is produced in plants and mimics one or more epitopes of antigen uniquely expressed by cells of tumor.
 DERWENT CLASS: B04 D16
 INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H;
 TUSE, D
 PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I)
 REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D
 COUNTRY COUNT: 1
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|------|--------------------|------|----|----|
| US 2003044417 | A1 | 20030306 (200343)* | | | 37 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|----------------|-----------------------------------|----------------------|
| US 2003044417 | A1 Provisional | US 1999-155979P
US 2000-539382 | 19990924
20000331 |

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US
 2000-539382 20000331

AN 2003-456551 [43] WPIDS
 CR 2001-596903 [67]; 2003-456552 [43]; 2003-492106 [46]; 2003-492153 [46]
 AB US2003044417 A UPAB: 20030928

NOVELTY - A polypeptide self-antigen (I) useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded by a nucleic acid (NA) in the cells of the tumor, including an epitope to, or overexpressed by tumor cells; produced in a cell or organism that has been transfected with NA and in a correctly folded form;

and capable of inducing an immune response in a mammal, is new.

DETAILED DESCRIPTION - (I) is useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, which polypeptide:

(1) includes an epitope or epitopes unique to, or overexpressed by, cells of the tumor, thus distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(2) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(3) is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form;

(4) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

(1) an individual-specific immunogenic product (II) comprising (I), produced by a method which involves joining a nucleic acid encoding the first domain of the polypeptide to a nucleic acid encoding a first part of a **linker** to produce a first nucleic acid construct, joining the nucleic acid encoding a second part of the **linker** to a nucleic acid encoding the second domain of the polypeptide to produce a second nucleic acid construct, incorporating the first and the second constructs into a transient plant expression vector in frame so that, when expressed, the polypeptide bears the first and second domain separated by the **linker**, transfecting a plant with the vector so that the plant transiently produces the polypeptide, and recovering the polypeptide as a soluble, correctly-folded protein;

(2) a vaccine composition (III) useful for inducing a tumor specific immune response, idiotype-specific anti-lymphoma immune response, and polyclonal immune response to an idiotype of a surface immunoglobulin or to an idiotype in a mouse, comprising (I), and a pharmaceutical carrier or excipient; and

(3) production of (I).

ACTIVITY - Anti-tumor; Cytostatic.

MECHANISM OF ACTION - Vaccine (claimed); Inducer of immune response.

Treatment of lymphoma patient with the scFv polypeptide vaccine was demonstrated as follows. An idiotype-bearing scFv was produced from lymphoma cells of a human subject (designated JJ). JJ was subjected to immunization, and JJ's response was evaluated by laboratory tests and clinical observation. JJ's serum contained antibodies specific for the vaccine immunogen and reactive with a monoclonal Ig (that corresponded to the idiotypic lymphoma surface Ig). The antibodies were detected in an enzyme linked immunosorbent assay (ELISA) and by fluorescence activated cell sorter (FACS) analysis using cryopreserved lymphoma cells from JJ. JJ's peripheral blood T lymphocytes responded significantly in *in vitro* to the vaccine polypeptide (or to the lymphoma cells as stimulators) by proliferation, measured as ^{3}H - thymidine incorporation and by secretion of interferon- gamma . JJ's peripheral blood mononuclear cells also produced TNF alpha in response to these stimuli. JJ's clinical response was characterized by radiographic evidence of lack of tumor progression and gradual disappearance of the lymphoma. No radiographic or other clinical signs of relapse were evident over one year of observation.

USE - (I) is useful as a tumor-specific vaccine, especially a B-cell lymphoma-specific vaccine. (III) is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject, preferably human or a subject who had a tumor and was treated so that no tumor is clinically or radiographically evident, where the tumor is B-cell lymphoma (claimed).

L9 ANSWER 5 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2001-596903 [67] WPIDS
 CROSS REFERENCE: 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46];
 2003-492153 [46]
 DOC. NO. CPI: C2001-176650
 TITLE: Novel polypeptide vaccine produced in plants, useful for
 inducing an immune response to a self-antigen on the
 surface of certain tumor cells.
 DERWENT CLASS: B04 D16
 INVENTOR(S): REINL, S J; TURPEN, T H; LINDBO, J A; MCCORMICK, A A;
 TUSE, D
 PATENT ASSIGNEE(S): (LARG-N) LARGE SCALE BIOLOGY CORP; (MCCO-I) MCCORMICK A
 A; (TUSE-I) TUSE D
 COUNTRY COUNT: 95
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|--|--------------------|------|-----|----|
| WO 2001068682 | A1 | 20010920 (200167)* | EN | 89 | |
| RW: | AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TZ UG ZW | | | | |
| W: | AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW | | | | |
| AU 2001012019 | A | 20010924 (200208) | | | |
| EP 1263779 | A1 | 20021211 (200301) | EN | | |
| R: | AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI | | | | |
| JP 2003527399 | W | 20030916 (200362) | | 117 | |
| ZA 2002006798 | A | 20031126 (200402) | | 94 | |
| EP 1263779 | B1 | 20041215 (200482) | EN | | |
| R: | AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE | | | | |
| DE 60016806 | E | 20050120 (200510) | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|------------------|----------|
| WO 2001068682 | A1 | WO 2000-US28362 | 20001013 |
| AU 2001012019 | A | AU 2001-12019 | 20001013 |
| EP 1263779 | A1 | EP 2000-973516 | 20001013 |
| | | WO 2000-US28362 | 20001013 |
| JP 2003527399 | W | WO 2000-US28362 | 20001013 |
| | | JP 2001-567772 | 20001013 |
| ZA 2002006798 | A | ZA 2002-6798 | 20020826 |
| EP 1263779 | B1 | EP 2000-973516 | 20001013 |
| | | WO 2000-US28362 | 20001013 |
| DE 60016806 | E | DE 2000-00016806 | 20001013 |
| | | EP 2000-973516 | 20001013 |
| | | WO 2000-US28362 | 20001013 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|---------------|
| AU 2001012019 | A Based on | WO 2001068682 |
| EP 1263779 | A1 Based on | WO 2001068682 |
| JP 2003527399 | W Based on | WO 2001068682 |
| EP 1263779 | B1 Based on | WO 2001068682 |
| DE 60016806 | E Based on | EP 1263779 |
| | Based on | WO 2001068682 |

PRIORITY APPLN. INFO: US 2000-522900 20000310
AN 2001-596903 [67] WPIDS
CR 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46]; 2003-492153 [46]
AB WO 200168682 A UPAB: 20050211

NOVELTY - A polypeptide self-antigen (I) useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, is new.

DETAILED DESCRIPTION - (I) includes an epitope or epitopes unique to, or over expressed by, cells of the tumor, thereby distinguishing the tumor from all other tumors of the same or different histological type, or in the subject or in another member of the subject's species. (I) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject, is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form. (I) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

(1) an individual-specific immunogenic product (II) comprising (I);
(2) a vaccine composition (VC) useful for inducing a tumor-specific immune response, idiotype-specific anti-lymphoma immune response, a polyclonal immune response to at least one idiotype of a surface immunoglobulin or a polyclonal immune response to an idiotype in a mouse, comprising (I); and
(3) producing (I).

ACTIVITY - Cytostatic; immunostimulator. The idiotype-bearing self antigen was administered by successive subcutaneous injection of 0.5 mg of the antigen and ISAF-1 adjuvant to humans with low grade B-cell lymphoma. The patients were given additional injections once a month for 5 months and booster doses were given annually. The results indicated that at least 6 of the 20 patients showed both immunological and clinical, including radiographic, signs of therapeutic success. The sera had significant titers of antibodies specific for the idiotype of their lymphoma cells and ScFV polypeptide used for immunization. Clinically, no signs of tumor progression and a statistically significant prolonged disease free interval after vaccination compared to historical controls, were observed. PCR (polymerase chain reaction) analysis of lymphocyte DNA across bcl-2/Igh, a molecular marker of human lymphoma, further confirmed the successful treatment of the lymphoma.

MECHANISM OF ACTION - Polyclonal anti-idiotypic antibody response inducer; cell-mediated immune response inducer (claimed).

USE - VC is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject or a subject who had a tumor e.g. B-cell lymphoma, and was treated so that no tumor is clinically or radiographically evident. (I) is useful for inducing a protective antitumor immune response (claimed).

ADVANTAGE - (I) can be produced at high levels, easy to purify and can be appropriately folded to mimic the conformation of the native epitopes displayed at the tumor cell surface.

Dwg.0/5

L9 ANSWER 6 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-316135 [33] WPIDS
DOC. NO. CPI: C2001-097326
TITLE: Novel library of dual-domain nucleic acid molecules useful for producing dual-domain proteins, or idiotypic scFv vaccine useful for treating B-cell lymphoma.
DERWENT CLASS: B04 C06 D16

INVENTOR(S): LINDBO, J A; REINL, S J; TURPEN, T; REINL, S

PATENT ASSIGNEE(S): (LARG-N) LARGE SCALE BIOLOGY CORP

COUNTRY COUNT: 91

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|------|--|------|-----|----|
| WO 2001023543 | A1 | 20010405 (200133)* | EN | 77 | |
| | RW: | AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW | | | |
| | W: | AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW | | | |
| AU 2000076017 | A | 20010430 (200142) | | | |
| EP 1218501 | A1 | 20020703 (200251) | EN | | |
| | R: | AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI | | | |
| KR 2002059413 | A | 20020712 (200306) | | | |
| JP 2003510073 | W | 20030318 (200321) | | 103 | |
| ZA 2002002066 | A | 20030528 (200341) | | | 82 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|-----------------|----------|
| WO 2001023543 | A1 | WO 2000-US25965 | 20000922 |
| AU 2000076017 | A | AU 2000-76017 | 20000922 |
| EP 1218501 | A1 | EP 2000-965277 | 20000922 |
| | | WO 2000-US25965 | 20000922 |
| KR 2002059413 | A | KR 2002-703842 | 20020323 |
| JP 2003510073 | W | WO 2000-US25965 | 20000922 |
| | | JP 2001-526926 | 20000922 |
| ZA 2002002066 | A | ZA 2002-2066 | 20020313 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|---------------|
| AU 2000076017 | A Based on | WO 2001023543 |
| EP 1218501 | A1 Based on | WO 2001023543 |
| JP 2003510073 | W Based on | WO 2001023543 |

PRIORITY APPLN. INFO: US 1999-155978P 19990924

AN 2001-316135 [33] WPIDS

AB WO 200123543 A UPAB: 20010615

NOVELTY - A library (I) of dual-domain nucleic acid molecules, each having a first and a second domain that are separated and linked by a linker which is a member of a randomized library (RL) of linkers that vary in size and nucleotide sequence and consists of a repeated pattern (RP) of degenerate repeated triplet nucleotides, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a dual-domain nucleic acid molecule (II), selected from (I);
(2) a library (III) of dual-domain polypeptide molecules each described by the formula D1-L-D2, where D1 and D2 are polypeptide domains and L is a peptide or a polypeptide linker which is a member of RL;

(3) a library (IV) of multi-domain polypeptide molecules each comprising polypeptide domains D each pair of which is linked by a peptide or polypeptide linker L, each molecule being described by the

formula DxLy, where x = 2-20 and y = 1-19, with the condition that for any value of x:

- (i) y = x-1;
- (ii) D1 is bonded to a single C-terminal **linker**;
- (iii) the C-terminal-most D is bonded to a single N-terminal **linker**;
- (iv) each of D2-D19 are bonded to a N-terminal and a C-terminal **linker**; and
- (v) each L is a member of RL;
- (4) a dual-domain polypeptide molecule (V) selected from (III);
- (5) a multi-domain polypeptide molecule (VI) selected from (IV);
- (6) generating (I);
- (7) a population of dual-domain polypeptides (VIII) or a dual-domain polypeptide of the population, obtained by the above method;
- (8) producing (V);
- (9) a **linker** nucleic acid molecule or a sequence (IX) that joins two nucleic acid domains or two nucleic acid sequences encoding two polypeptide domains, which has a pattern of **degenerate repeated triplet** nucleotides, where all the three nucleotides at positions 1-3 are different, and the molecule or sequence that joins the domains does not encode Gly4Ser or its **repeat**;
- (10) a library (X) of (IX); and
- (11) making (X).

USE - (I) is useful for producing dual-domain proteins of interest that have therapeutic value, e.g., idiotypic scFv vaccine for treating B-cell lymphoma.

ADVANTAGE - The expression systems obtained by the above said methods are suitable for rapid and economical production of useful quantities of correctly folded polypeptides in surprisingly high abundance and potent immunogenicity.

Dwg.0/3

| | | | |
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 LAST RELOADED: Feb 18, 2005 (20050218/UP).

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 19:55:58 ON 23 FEB 2005

| | |
|----|--------------------------------------|
| L1 | E REINL STEPHEN?/AU |
| L2 | 16 E1 OR E2 |
| L3 | 6 L1 AND LINKER |
| L4 | 13 DUP REM L1 (3 DUPLICATES REMOVED) |
| | 4 L3 AND LINKER |

FILE 'STNGUIDE' ENTERED AT 19:59:13 ON 23 FEB 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 20:08:39 ON 23 FEB 2005

L5 9 L3 NOT L4

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 21:12:14 ON 23 FEB 2005

L6 6 LIBRARY AND DEGENERATE AND LINKER AND TRIPLET AND REPEAT?
L7 6 DUP REM L6 (0 DUPLICATES REMOVED)
L8 6 L7 NOT L1
L9 6 DEGENERATE AND LINKER AND TRIPLET AND REPEAT?
L10 0 L9 NOT L7
L11 8 LIBRARY AND LINKER AND TRIPLET AND REPEAT?
L12 2 L11 NOT L9
L13 38 LINKER AND TRIPLET AND REPEAT?
L14 18 DUP REM L13 (20 DUPLICATES REMOVED)
L15 14 L14 NOT L9
L16 12 L15 NOT L12
L17 11 L16 NOT L3
L18 11 L17 NOT L2
L19 11 L18 NOT L6

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 0.18 | 147.42 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -2.92 |

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